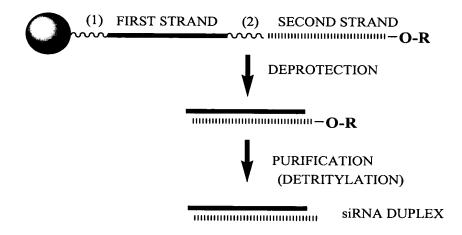
Inventor's Name: McSwiggen et al.

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# Figure 1



= SOLID SUPPORT

R = TERMINAL PROTECTING GROUP FOR EXAMPLE: DIMETHOXYTRITYL (DMT)

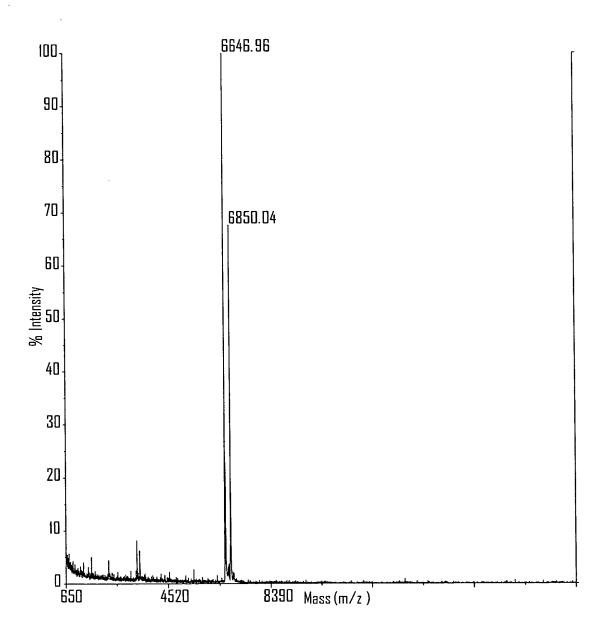
= CLEAVABLE LINKER
(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
(2) INVERTED DEOXYABASIC SUCCINATE)
= CLEAVABLE LINKER

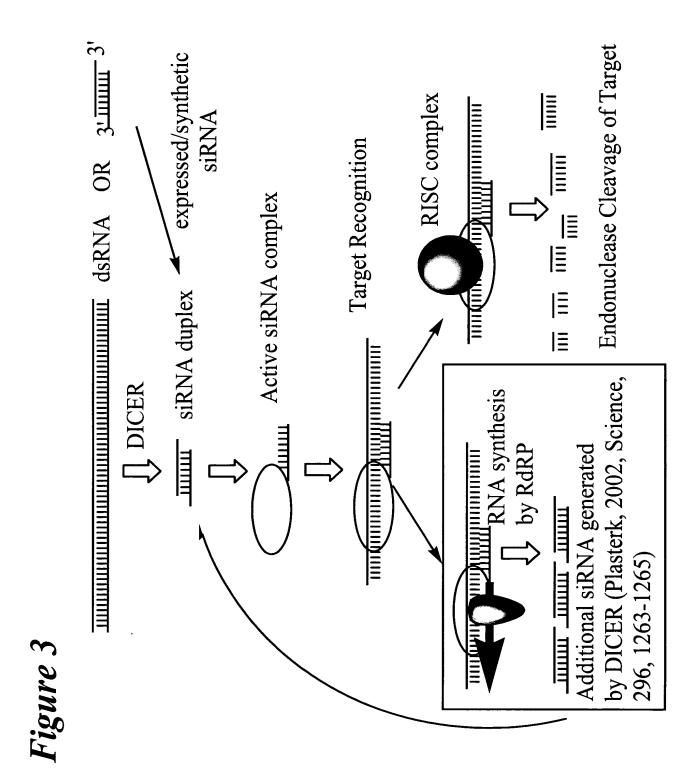
(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR INVERTED DEOXYABASIC SUCCINATE)

INVERTED DEOXYABASIC SUCCINATE LINKAGE

GLYCERYL SUCCINATE LINKAGE

Figure 2





### Figure 4

A	SENSE STRAND (SEQ ID NO 207) ALL POSITIONS RIBONUCLEOTIDE EXCEPT POSITIONS (N N)  5'- B-N N N N N N N N N N N N N N N N N N	-3'	
	)	-5'	۲
	ANTISENSE STRAND (SEQ ID NO 208) ALL POSITIONS RIBONUCLEOTIDE EXCEPT POSITIONS (N N)	_	
В	SENSE STRAND (SEQ ID NO 209) ALL PYRIMIDINES = 2'-FLUORO AND ALL PURINES = 2'-OM EXCEPT POSITIONS (N N	J) ¬	
	(- 3)	3'	
	$\frac{1}{3}$ '- L-(N <sub>s</sub> N) NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	-5'	۲
	ANTISENSE STRAND (SEQ ID NO 210) ALL PYRIMIDINES = 2'-FLUORO AND ALL PURINES = 2'-O-ME EXCEPT POSITIONS (N	N)	
C	SENSE STRAND (SEQ ID NO 211)	)	١
	ALL PYRIMIDINES = 2'-O-ME OR 2'-FLUORO EXCEPT POSITIONS (N N)		
	2	-3'	٢
	3'- L-(N <sub>s</sub> N) N N N N N N N N N N N N N N N N N N	-5'	
	ANTISENSE STRAND (SEQ ID NO 212) ALL PYRIMIDINES = 2'-FLUORO EXCEPT POSITIONS (N N)	J	
D	SENSE STRAND (SEQ ID NO 213) ALL PYRIMIDINES = 2'-FLUORO EXCEPT POSITIONS (N N) AND ALL PURINES = 2'-DEC	xy	
	5'- B-NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	.3'	L
	$\int 3'$ - L- $(N_sN)$ NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	5'	
	ANTISENSE STRAND (SEQ ID NO 210) ALL PYRIMIDINES = 2'-FLUORO AND ALL PURINES = 2'-O-ME EXCEPT POSITIONS (N	N)	
E	SENSE STRAND (SEQ ID NO 214) ALL PYRIMIDINES = 2'-FLUORO EXCEPT POSITIONS (N N)	)	
	5'- B-NNNNNNNNNNNNNNNNNNNN (NN)-B -	3'	
	$\begin{cases} 3'- L-(N_sN)NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN$	5' }	<b>&gt;</b>
	ANTISENSE STRAND (SEQ ID NO 210) ALL PYRIMIDINES = 2'-FLUORO AND ALL PURINES = 2'-O-ME EXCEPT POSITIONS (N	N)	
	GENCE CTRAND (GEO ID NO 212)	٦	
	SENSE STRAND (SEQ ID NO 213) ALL PYRIMIDINES = 2'-FLUORO EXCEPT POSITIONS (N N) AND ALL PURINES = 2'-DEO	XY	
F	J 5'- B-NNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	.3' \	<b>&gt;</b>
	$3'$ - L- $(N_sN)$ N N N N N N N N N N N N N N N N N N	-5' [	
	ANTISENSE STRAND (SEQ ID NO 215) ALL PYRIMIDINES = 2'-FLUORO EXCEPT POSITIONS (N N) AND ALL PURINES = 2'-DEO	xγJ	

POSITIONS (NN) CAN COMPRISE ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (eg. THYMIDINE) OR UNIVERSAL BASES

B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT

L = GLYCERYL MOIETY THAT IS OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE

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# Figure 5

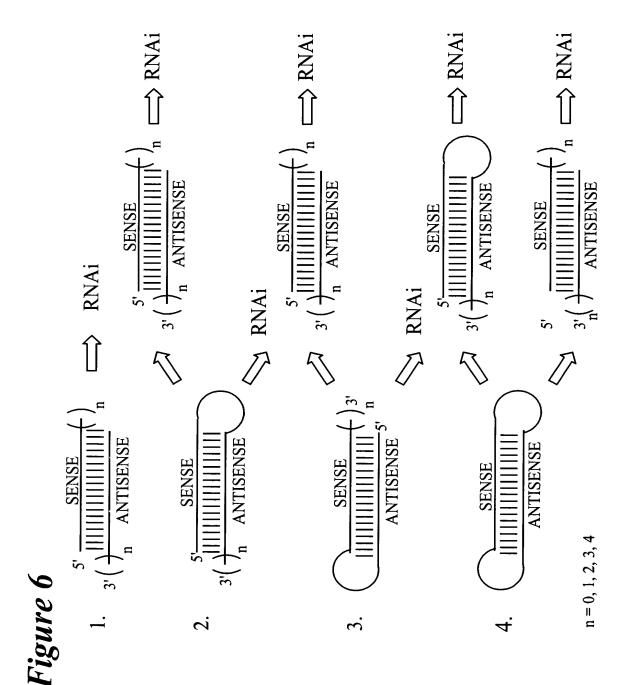
			_
		SENSE STRAND (SEQ ID NO 216)	
A	5'-	iB-G C C G C U U C G A G C G G A U G C U T T-iB	-3'
	\ <sub>3'-</sub>	L-T <sub>S</sub> TCGGCGAAGCUCGCCUACGA	-5' }
		ANTISENSE STRAND (SEQ ID NO 217)	_
		ANTISENSE STRAND (SEQ ID NO 217)	
		SENSE STRAND (SEQ ID NO 218)	j
В	5'-	g c c g c u u c g <u>a</u> g c g g <u>a</u> u g c u T T	-3'
	<b>√</b> 3'-	L-T <sub>S</sub> T c g g c g <u>a</u> <u>a</u> g c u c g c c u <u>a</u> c g <u>a</u>	-5' >
		ANTISENSE STRAND (SEQ ID NO 219)	
		MITTISENSE STICKED (SEQ ID NO 219)	
		SENSE STRAND (SEQ ID NO 220)	7
		SENSE STRAIN (SEQ ID NO 220)	
C	5'-	iB-G c c G c u u c G A G c G G A u G c u T T-iB	-3'
	<b>₹ 3'-</b>	L-T <sub>S</sub> T c G G c G A A G c u c G c c u A c G A	-5' }
	ļ	ANTISENSE STRAND (SEQ ID NO 221)	
			Ś
D		SENSE STRAND (SEQ ID NO 222)	
	5'-	iB-GccGcuucGAGcGGAuGcuTT-iB	-3'
	\(\frac{3}{2}\)-	L-T <sub>S</sub> T c g g c g <u>a</u> <u>a</u> g c u c g c c u <u>a</u> c g <u>a</u>	-5' >
		ANTISENSE STRAND (SEQ ID NO 219)	
		111(11021)22 0110 113 (02 (22 110 21))	
	7	SENSE STRAND (SEQ ID NO 223)	Ź
			21
יתו	3-	iB-G c c G c u u c G A G c G G A u G c u T T-iB	-3'
E	3'-	L-T <sub>S</sub> T c g g c g <u>a</u> <u>a</u> g c u c g c c u <u>a</u> c g <u>a</u>	-5' >
		ANTISENSE STRAND (SEQ ID NO 219)	
			J
		SENSE STRAND (SEQ ID NO 222)	)
	5'-	iB-GccGcuucGAGcGGAuGcuTT-iB	-3'
F	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	L-T <sub>S</sub> T c G G c G A A G c u c G c c u A c G A	-5' }
•	] ]-	•	-5
		ANTISENSE STRAND (SEQ ID NO 224)	
			J

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro | ITALIC UPPER CASE = DEOXY italic lower case = 2'-deoxy-2'-fluoro <u>underline</u> = 2'-O-methyl

**B = INVERTED DEOXYABASIC** 

L = GLYCERYL MOIETY OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE ORPHOSPHORODITHIOATE

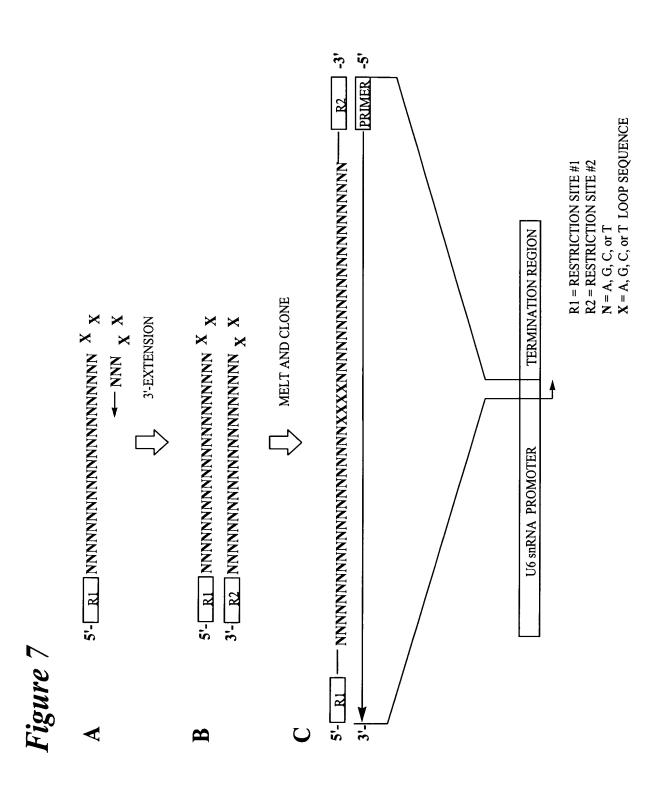


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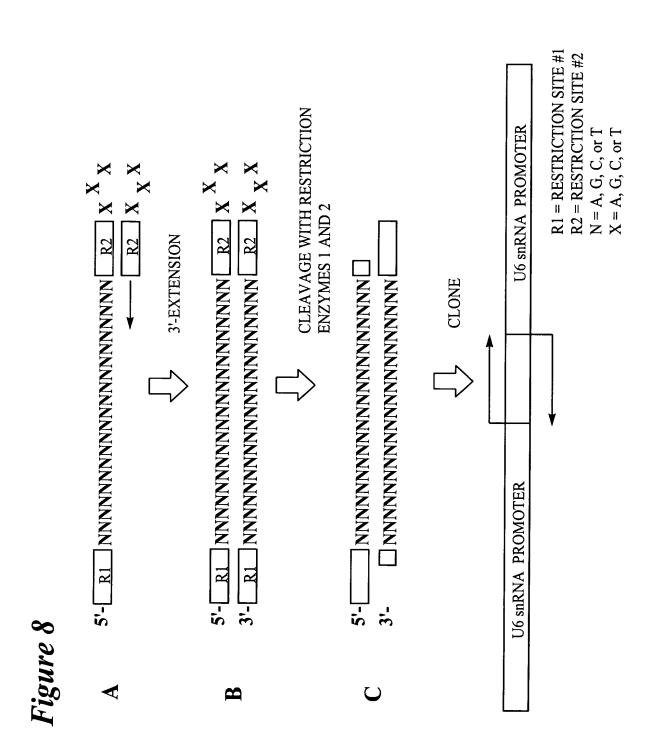
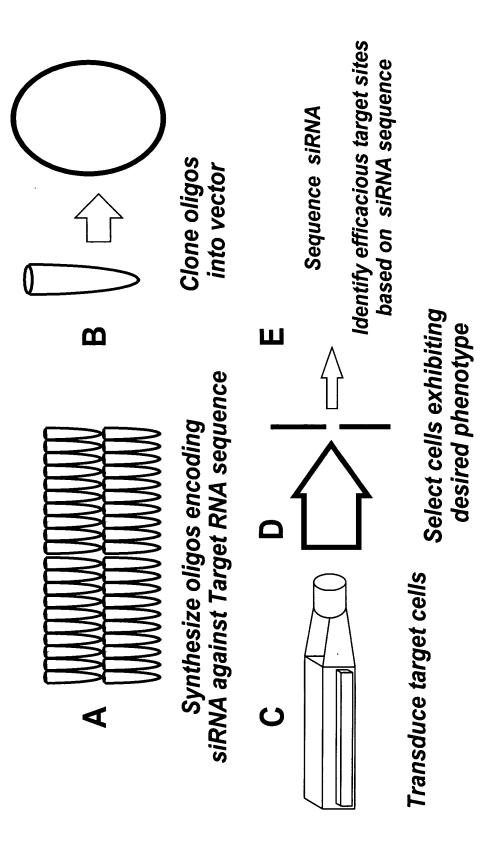


Figure 9: Target site Selection using siRNA



# 9 CH<sub>3</sub>O 0=P-R P O œ :오 9

R = O, S, N, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl B = Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

luciferase reporter Test for activity in system Figure 11: Modification Strategy Compare stability and activity vs unmodified construct Make an educated modification stability in human serum Test for nuclease